IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

Laskey et al Atty. Ref.: **620-161**

Divisional of Serial No. **09/175,947** Group:

Filed: **August 7, 2001** Examiner:

For: **DETECTION OF DYSPLASTIC OR NEOPLASTIC CELLS USING ANTI-MCM2 ANTIBODIES**

* * * * * * * * * * * *

August 7, 2001

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

PRELIMINARY AMENDMENT

Preliminarily amend the above-identified application as follows:

IN THE TITLE

Amend the title to read as follows:

--DETECTION OF DYSPLASTIC OR NEOPLASTIC CELLS USING ANTI-MCM2 ANTIBODIES--.

IN THE SPECIFICATION

Amend the specification as follows:

Page 15, delete the paragraph spanning lines 19 and 20 and insert the following therefor:

--Human MCM6 sequence is disclosed in Holthoff et al, 1996, *Genomics*, **37**, 131-134, GenBank Acc. No. U46838.--

Page 36, delete the paragraph spanning lines 18-20 and insert the following therefor:

--The present inventors have also shown by Western blot that Cdc6 expression is down-regulated when mouse 3T3 fibroblasts are made quiescent by contact inhibition.--

Page 57, delete the paragraph spanningn lines 16-19, and insert the following therefor:

--The peptide VVCIDEFDKMSDMRTAC (SEQ ID NO:1), corresponding to a consensus sequence common to the MCM family of proteins, was synthesized using t-BOC chemistry. The peptide was conjugated to PPD (purified protein derivative – tuberculin).--

Page 75, delete Table 1 and insert the following therefor:

--Comparison of anti-Mcm5 antibody test versus conventional Pap test in a blind trial of patients recalled to colposcopy clinics

		Standard Pap test result		
		Normal	Low grade	High grade
Anti-Mcm5 antibody test	Presence of positive cells	3[a]	9	17
	Absence of positive cells	13	0	0

a) see text --

Insert the attached Sequence Listing after the claims pages.

IN THE CLAIMS

Cancel claims 1-87, without prejudice.

Add the following claims:

--88. (new) A method of determining the presence or absence of dysplastic or neoplastic cells in a test sample from an individual, the method comprising:

contacting the test sample with an antibody or antibody fragment directed against Minichromosome Maintenance protein 2 (MCM2 protein); and

determining amount and/or pattern of binding of said antibody or antibody fragment to said test sample;

whereby an increase in said amount and/or a difference in said pattern if detected for the test sample compared with normal is indicative of presence of dysplastic or neoplastic cells in said test sample.

89. (new) A method according to claim 88 wherein binding of said antibody or antibody fragment to MCM2 protein in the test sample is indicative of the presence of dysplastic or neoplastic cells in said test sample.

90. (new) A method according to claim 88 wherein a difference in pattern of binding of said antibody or antibody fragment to said test sample compared with normal is indicative of the presence of dysplastic or neoplastic cells in said test sample.

91. (new) A method according to claim 88 wherein a sample of tissue is tested.

92. (new) A method according to claim 91 wherein the sample of tissue is fresh or frozen.

93. (new) A method according to claim 91 wherein the sample of tissue is not formalin fixed or paraffin embedded.

94. (new) A method according to claim 91 wherein the sample of tissue is not the subject of antigen retrieval or pressure cooking/autoclaving.

95. (new) A method according to claim 91 wherein the tissue is selected from lung, breast, colon, prostate, stomach, skin, oesophagus and bladder.

96. (new) A method according to claim 92 wherein the tissue is selected from lung, breast, colon, prostate, stomach, skin, oesophagus and bladder.

97. (new) A method according to claim 93 wherein the tissue is selected from lung, breast, colon, prostate, stomach, skin, oesophagus and bladder.

98. (new) A method according to claim 91 wherein the tissue is breast tissue.

99. (new) A method according to claim 92 wherein the tissue is breast tissue.

100. (new) A method according to claim 88 wherein a sample of cells is tested.

101. (new) A method according to claim 88 wherein the sample is provided from fluid taken from the individual.

102. (new) A method according to claim 101 wherein a sample of cells is provided from said fluid.

103. (new) A method according to claim 101 wherein the fluid is blood.

104. (new) A method according to claim 101 wherein the fluid is urine.

105. (new) A method according to claim 88 wherein a population of individuals is screened.

106. (new) A method of determining the presence or absence of dysplastic or neoplastic cells in a test cervical sample from an individual, the method comprising:

contacting the test cervical sample with an antibody or antibody fragment directed against Minichromosome Maintenance protein 2 (MCM2); and

determining an amount and/or pattern of binding of said antibody or antibody fragment to said test cervical sample;

whereby an increase in said amount and/or a difference in said pattern if detected for the test cervical sample compared with normal is indicative of presence of dysplastic or neoplastic cells in said test cervical sample.

107. (new) A method according to claim 106 wherein the sample is a cervical smear.

108. (new) A method according to claim 107 wherein binding of said antibody or antibody fragment to MCM2 protein in the cervical smear is indicative of the presence of dysplastic or neoplastic cells in said cervical smear.

109. (new) A method according to claim 106 wherein a population of individuals is screened.--

REMARKS

Claims 1-87 have been canceled, without prejudice.

Claims 88-109 have been added and are pending.

The specification has been amended, as provided in the parent application Serial No. 09/175,947. No new matter has been added.

The specification has been amended to include the attached Sequence Listing. The attached paper copy of the Sequence Listing is the same as the paper and computer-readable copies of the Sequence Listing filed in the parent application Serial No. 09/175,947. The Office is requested to use the computer-readable copy of the

Sequence Listing from the parent application from Serial No. 09/175,947 for the present case. See, attached Request. No new matter has been added.

Early passage of the subject application to issue is earnestly solicited.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: ______________________

B. J. Sadoff
Reg. No. **36,663**

BJS:eaw
1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

MARKED UP SPECIFICATION PAGES

Amend the specification as follows:

Page 15, delete the paragraph spanning lines 19 and 20

[Human MCM6 sequence is disclosed in Holthoff et al, 1996, *Genomics*, **37**, 131-134, GenBank Acc. No. X67334.]

and insert the following therefor:

--Human MCM6 sequence is disclosed in Holthoff et al, 1996, *Genomics*, **37**, 131-134, GenBank Acc. No. U46838.--

Page 36, delete the paragraph spanning lines 18-20

[The present inventors have also shown by Western blot that Cdc6 expression is down-regulated when mouse 3T3 fibroblasts are made quiescent by contact inhibition (Figure 1A).]

and insert the following therefor:

--The present inventors have also shown by Western blot that Cdc6 expression is down-regulated when mouse 3T3 fibroblasts are made quiescent by contact inhibition.--

Page 57, delete the paragraph spanning lines 16-19,

[The peptide VVCIDEFDKMSDMRTAC, corresponding to a consensus sequence common to the MCM family of proteins, was synthesized using t-BOC chemistry. The peptide was conjugated to PPD (purified protein derivative – tuberculin).]

and insert the following therefor:

--The peptide VVCIDEFDKMSDMRTAC (SEQ ID NO:1), corresponding to a consensus sequence common to the MCM family of proteins, was synthesized using t-

BOC chemistry. The peptide was conjugated to PPD (purified protein derivative – tuberculin).--

Page 75, delete Table 1

[Comparison of anti-Mcm5 antibody test versus conventional Pap test in a blind trial of patients recalled to colposcopy clinics

		Standard Pap test result		
		Normal	Low grade	High grade
Anti-Mcm5 antibody test	Presence of +ve cells	3[a]	9	17
	Absence of +ve cells	13	0	0

a) see text]

and insert the following therefor:

--Comparison of anti-Mcm5 antibody test versus conventional Pap test in a blind trial of patients recalled to colposcopy clinics

		Standard Pap test result		
		Normal	Low grade	High grade
Anti-Mcm5 antibody test	Presence of positive cells	3[a]	9	17
	Absence of positive cells	13	0	0

a) see text--